

**ABSTRACT**

Methods for obtaining antisense oligonucleotides with activity against a desired target are provided. Methods of identifying oligonucleotide sequence motifs which are  
5 predictive of antisense oligonucleotide activity are provided, as are motifs identified according to this method. Methods of selecting effective antisense oligonucleotide sequences and effective antisense target sequences are provided, as are sequences selected according to these methods. In other  
10 methods of the invention, oligonucleotides are designed to hybridize to target sequences containing one or more activity-enhancing motifs. Antisense oligonucleotides designed according to these methods are also provided.